



Do specific types of sleep disturbances represent risk factors for poorer health-related quality of life in inflammatory bowel disease? A longitudinal cohort study

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Objectives. Poor global sleep quality is commonly reported in people with inflammatory bowel disease (IBD) and is linked to poorer health-related quality of life (HRQoL). However, understanding is currently limited by a lack of: (1) longitudinal research and (2) research investigating the impact of specific types of problems sleeping on IBD-related outcomes, particularly on HRQoL.

Design. Observational longitudinal cohort study.

Methods. $N = 276$ participants with IBD completed measures at baseline (T1) and 4 weeks later at T2. Four specific sleep disturbances associated with IBD including sleep apnoea, insomnia, restless legs, and nightmares were measured alongside depression, anxiety and stress, and HRQoL.

Results. After controlling for participant demographics and clinical characteristics, T1 depression, anxiety, stress, and T1 HRQoL, more severe symptom severity of sleep apnoea ($B = -0.30, p < .05$) and insomnia symptoms ($B = -0.23, p < .05$) at T1 significantly predicted poorer HRQoL at T2. However, the experience of restless legs ($B = -0.03, p > .87$) and nightmares ($B = -0.14, p > .11$) at T1 did not predict HRQoL.

Conclusion. Symptoms synonymous with sleep apnoea and insomnia might represent modifiable risk factors that provide independent contributions to HRQoL over time in those with IBD. These findings suggest that interventions designed to improve sleep apnoea and insomnia could confer benefits to HRQoL in those with IBD. However, more longitudinal research is needed to understand the contribution of sleep disturbances over the longer term, as well as more randomized controlled trials testing the effect of improving sleep on IBD-related outcomes.

Statement of contribution

What is already known on this subject?

- Poor global sleep quality is commonly reported by those with a diagnosis of inflammatory bowel disease.

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- Poor global sleep quality is adversely associated with a number of IBD-related outcomes including quality of life, fatigue, and disease symptom flares.
- However, extant literature has not examined the contribution of *specific* types of sleep disturbances to health-related quality of life in IBD over time, instead relying on global measures of sleep, and largely limited to cross-sectional designs.

What does this study add?

- To our knowledge, this is the first longitudinal study investigating whether specific types of sleep disturbances known to be associated with IBD-related outcomes can predict subsequent HRQoL in IBD.
- Specific symptoms of sleep apnoea and insomnia (but not restless legs or nightmares) might represent risk factors for HRQoL over time in those with IBD.

Inflammatory bowel disease (IBD), including the two main diagnoses of Crohn's disease (CD) and ulcerative colitis (UC), is a chronic condition characterized by relapsing and remitting inflammation of the gastrointestinal tract and is a global health concern (M'Koma, 2013) that has huge implications for both the individuals affected by IBD, and the health care systems charged with providing care (Odes *et al.*, 2006; Park & Bass, 2011). The pathogenesis of IBD is complex; however, it is accepted to include a combination of genetic, environmental, and behavioural factors (Ananthakrishnan, 2013, 2015; Xavier & Podolsky, 2007). Given that the environmental and behavioural risk factors associated with IBD are more amenable to change, there has been an upsurge in attempts to target these risk factors as a route to improving IBD and its related outcomes. One such modifiable behavioural risk factor commonly associated with IBD that has received attention in recent years is sleep (Ali & Orr, 2014; Ananthakrishnan, 2015; Kinnucan, Rubin, & Ali, 2013).

Sleep disturbances in IBD

The majority of extant literature investigating the role of sleep in IBD has tended to measure 'sleep quality', which is generally accepted to consist of two domains: (1) sleep continuity (i.e., getting to sleep and staying asleep through the night) and (2) feeling refreshed upon waking (Harvey, Stinson, Whitaker, Moskovitz, & Virk, 2008; Libman *et al.*, 2016). Generally, people living with IBD report poorer self-reported sleep quality when compared to healthy controls (Iskandar *et al.*, 2020; Keefer, Stepanski, Ranjbaran, Benson, & Keshavarzian, 2006; Kinnucan *et al.*, 2013; Qazi & Farraye, 2018; Ranjbaran *et al.*, 2007). Getting good quality sleep is important in its own right. For example, in a survey of over 8,000 people from the general population, good quality sleep was the single biggest contributor to well-being, more than job security, income, and relationship status (National Centre for Social Research, 2017). However, getting good quality sleep might be particularly important for those with IBD, with a handful of longitudinal studies suggesting that poor sleep quality is associated with poorer clinical outcomes, including fatigue (Graff *et al.*, 2013) and disease activity (Ananthakrishnan, Long, Martin, Brendel, & Kappelman, 2013; Uemura *et al.*, 2016). Sleep quality is, therefore, an important and widely reported construct within IBD research. However, measuring overall sleep quality, and/or its constituent parts, is unable to accurately delineate whether *specific* types of sleep disturbance (e.g., insomnia) might be associated with IBD-related outcomes. Given that people with IBD experience a variety of specific sleep disturbances (Scott, Flowers, & Rowse, 2020), including symptoms of sleep apnoea (Keefer *et al.*, 2006; Ranjbaran *et al.*, 2007), insomnia (Hon, 2010; Ranjbaran *et al.*, 2007), restless-leg syndrome (Becker *et al.*,

2018; Takahara *et al.*, 2017), and nightmares (Pirinen, Kolho, Simola, Ashorn, & Aronen, 2010; Ranjbaran *et al.*, 2007), it is important that the associations between sleep and IBD are broken down further, with the study of specific disturbances and IBD outcomes.

Health-related quality of life in IBD and the association with sleep disturbance

One outcome that is particularly affected by IBD is health-related quality of life (HRQoL), which refers to 'those aspects of self-perceived well-being that are related to or affected by the presence of disease or treatment' (Ebrahim, 1995, p. 1384). For example, Devlen *et al.* (2014) reported that the symptoms of IBD can provoke both immediate impacts on HRQoL (e.g., disruption of daily activities, dietary restrictions, lifestyle changes) and more distal impacts (e.g., work, school, social and leisure activities, relationships, and psychological well-being). Given that it is currently not possible to 'cure' IBD, the goal of treatment is often to achieve and maintain control of the disease, thereby optimizing HRQoL (Bodger, Ormerod, Shackcloth, & Harrison, 2014). Consequently, IBD HRQoL is an important outcome, to both patients receiving care and to the clinicians who provide it (Huppertz-Hauss *et al.*, 2015). However, the finding from a recent meta-analysis that disease symptom activity explains only 37% of the variance in HRQoL in those with CD has led to calls for more research into additional, possibly modifiable determinants of HRQoL in those with IBD (van der Have *et al.*, 2014). Given that sleep has been shown to be a modifiable determinant of health in a number of fields (Kyle & Henry, 2017; Kyle, Morgan, & Espie, 2010), it is possible that sleep might represent a risk factor for HRQoL in those with IBD. However, only a small number of studies limited by a cross-sectional design and smaller sample sizes have investigated the association between sleep and IBD HRQoL, many of which report that that poor sleep quality is associated with poorer HRQoL (Habibi *et al.*, 2017; Keefer *et al.*, 2006; Ranjbaran *et al.*, 2007; Uemura *et al.*, 2016).

The present research

The present research aims to build on extant literature by addressing two key limitations. Firstly, the majority of extant literature has focussed on measuring overall sleep quality; therefore, it is unclear whether *specific* types of problems sleeping might be more or less associated with IBD-related outcomes. Given that different types of sleep disturbances have different screening methods (Devine, Hakim, & Green, 2005; Ibáñez, Silva, & Cauli, 2018; Marino *et al.*, 2013) and treatment strategies (Hansen, Höfling, Kröner-Borowik, Stangier, & Steil, 2013; Harrison, Keating, & Morgan, 2019; Iftikhar *et al.*, 2017; Zachariae, Lyby, Ritterband, & O'Toole, 2016), understanding whether specific types of sleep disturbances are predictive of HRQoL in IBD could facilitate suggestions that health care services should be doing more to screen for and subsequently treat sleep disturbances as part of routine care (Almedimigh *et al.*, 2018; Green *et al.*, 2017; Kinnucan *et al.*, 2013; Sofia *et al.*, 2018). Secondly, no study has examined the temporal relationship between specific sleep disturbances and HRQoL in those with IBD over time. In an effort to address these limitations, we will measure specific types of sleep disturbances that previous literature has suggested are associated with IBD including symptoms of sleep apnoea, insomnia, restless legs, and nightmares. Then, we will test whether these sleep disturbances can predict HRQoL 4 weeks later. We hypothesize that baseline symptoms of these sleep disturbances will all predict HRQoL at follow-up.

Method

Study design

The present research adopted a longitudinal cohort design. Participants completed self-reported measures. All measurements were taken online at baseline (T1) and then again 4 weeks later (T2). Ethical approval for this research was provided by the Research Ethics Committee based within the School of Health and Related Research (SchARR), at the University of Sheffield.

Participants

Participants were recruited from two sources: (1) through the 'Crohn's and Colitis UK' charity website, and (2) from online support groups for those living with IBD. Enrolment to the study began in May 2017 and concluded in July 2017. The inclusion criteria for the present research required participants to be: (1) over the age of sixteen (so that consent could be obtained from the participant alone), and (2) have a diagnosis of IBD. Participants not meeting these two criteria, not providing explicit electronic consent, those who did not provide a follow-up email address so their responses could be linked at T2, and those who did not start the baseline surveys were excluded from the present study.

Measures

Demographic and clinical characteristics

Participants were asked their age and gender, as well as items pertaining to their IBD including their IBD diagnosis type, age at IBD diagnosis, number of years living with an IBD diagnosis, number of IBD-related hospital admissions in the past year, whether they had ever undergone IBD-related surgery, current and/or previous use of a stoma, and whether they were currently taking medication for their IBD. Additionally, participants were asked whether they were currently receiving psychological therapy and/or medication for a mental health or sleep-related problem. These variables were chosen to not only describe the characteristics of the sample, but also because they are characteristics that might be associated with sleep, depression, anxiety, stress, and HRQoL (and therefore might require controlling for in the analyses).

The Sleep-50 Questionnaire

The Sleep-50 was used to measure symptoms of four types of sleep disturbance, including symptoms of (1) sleep apnoea (e.g., 'I'm sometimes short of breath when I wake up during the night'); (2) insomnia (e.g., 'I find it difficult to fall asleep'); (3) restless legs (e.g., 'I cannot keep my legs still when I'm falling asleep'); and (4) nightmares (e.g., 'I have frightening dreams'). Participants are asked the extent to which each item has applied to them over the previous 4 weeks on a 4-point scale ranging from 1 (not at all) to 4 (very much), with higher scores indicating more severe sleep disturbance. The Sleep-50 has been validated for use in both the general population and those with clinically defined sleep complaints (Spoormaker, Verbeek, van den Bout, & Klip, 2005). Internal reliability in the present research was acceptable for the sleep apnoea ($\alpha = 0.72$), and restless legs subscales ($\alpha = 0.76$), good for the insomnia subscale ($\alpha = 0.87$), and excellent for the nightmares subscale ($\alpha = 0.94$).

The Short Form Depression, Anxiety, Stress Scale (DASS-21)

Depression, anxiety, and stress were measured using the 21-item short form of the Depression, Anxiety, and Stress Scale (DASS-21). Participants are asked to indicate on a 4-point scale ranging from 0 to 3, the extent to which they agreed with statements assessing facets of negative affect over the past week. For example, seven statements are concerned with feelings of depression (e.g., 'I couldn't seem to experience any positive feeling at all'). A further seven statements ask participants about feelings of anxiety (e.g. 'I was aware of the action of my heart'). Finally, seven statements aim to explore feelings of stress (e.g. 'I was intolerant of anything that kept me from getting on'). The lowest possible total score on the DASS-21 is 0, through to 63, with higher scores indicating higher levels of negative affect.

To calculate severity cut-offs for the DASS-21, total scores for each subscale were multiplied by two (so that scores are comparable to the DASS-42, Ng *et al.*, 2007), and cut-offs suggested by Lovibond and Lovibond (1995) were used to assign a qualitative index. For total depression, the 'normal' range = 0–9, 'mild' = 10–13, 'moderate' = 14–20, 'severe' = 21–27, and 'extremely severe' = 28+. For total anxiety, the 'normal' range = 0–7, 'mild' = 8–9, 'moderate' = 10–14, 'severe' = 15–19, and 'extremely severe' = 20+. For total stress, the 'normal' range = 0–14, 'mild' = 15–18, 'moderate' = 19–25, 'severe' = 26–33, and 'extremely severe' = 34+. The DASS-21 has been validated for use in both clinical and non-clinical populations and has been found to be a reliable and valid measure of negative affect (Henry & Crawford, 2005). In the present research, internal reliability was excellent for the depression scale ($\alpha = 0.93$) and good for the stress ($\alpha = 0.87$), and anxiety scales ($\alpha = 0.82$).

The Short Inflammatory Bowel Disease Questionnaire (SIBDQ)

The SIBDQ is a 10-item measure of the HRQoL of those with IBD and is comprised of items derived from its longer form, the Inflammatory Bowel Disease Questionnaire (IBDQ, Guyatt *et al.*, 1989). The SIBDQ measures four domains of IBD HRQoL: (1) bowel symptom frequency (e.g., 'how often during the last 2 weeks have you been troubled by pain in the abdomen?'), (2) social aspects (e.g., 'how often during the last 2 weeks have you had to delay or cancel a social engagement because of your bowel problem?'), (3) systemic (e.g., 'overall, in the last 2 weeks, how much of a problem have you had maintaining or getting to the weight you would like to be?'), and (4) emotional (e.g., 'how much of the time during the last 2 weeks have you felt angry as a result of your bowel problem?'). Participants are asked to rate the extent to which each item has applied to them over the last 2 weeks using a 7-point scale, where 1 = all of the time and 7 = none of the time. Total scores range from 10 to 70, with lower scores indicating more impaired IBD HRQoL. The SIBDQ is a valid and reliable measure of HRQoL in those with IBD (Jowett, Seal, Barton, & Welfare, 2001). Internal reliability of the SIBDQ in the present research was good ($\alpha = 0.81$).

Approach to analysis

Hierarchical multiple linear regression analysis was conducted using SPSS v25 (IBM, 2017) to test whether symptom severity of sleep apnoea, insomnia, restless legs, and/or nightmares at T1 could predict HRQoL 4 weeks later at T2 (while controlling for T1 depression, anxiety, stress, and HRQoL).

Variables included in the analysis

The dependent variable in the present research was HRQoL as measured by the SIBDQ at T2. The independent variables included in the analysis were T1 symptoms of sleep apnoea, insomnia, restless legs, and nightmares. The analysis also included a number of covariates likely to confound the relationship. Firstly, any T1 participant demographic or clinical characteristic variable that significantly correlated with the independent and/or dependent variables in the model were entered as covariates, including age, gender, number of years living with an IBD diagnosis, diagnosis type (CD or UC), and the number of IBD-related hospital admissions in the last year. Secondly, given that depression, anxiety, and stress are associated with both sleep disturbances (Alvaro, Roberts, & Harris, 2013; Baglioni *et al.*, 2011; Taylor, Lichstein, Durrence, Reidel, & Bush, 2005), and HRQoL (Darchia *et al.*, 2018; Kyle *et al.*, 2010; Lee *et al.*, 2009), depression, stress, and anxiety at T1 were entered as a covariate in the model. Finally, it is likely that T1 HRQoL will be the strongest predictor of T2 HRQoL; therefore, T1 HRQoL was entered as a covariate in the model.

Sample size calculations

Sample size calculations were performed using G*Power 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007). To detect a small- to-medium-sized effect with 80% power, a significance threshold of $p < .05$, a minimum sample size of $N = 250$ was required.

Results

Participants and missing data

Figure 1 describes the flow of participants through the study. $N = 498$ participants began the online eligibility and consent procedures, of which $N = 16$ did not meet the inclusion criteria ($N = 9$ under 16 years old, $N = 7$ had no IBD diagnosis), $N = 22$ did not provide consent, $N = 29$ did not provide an email address, and $N = 22$ did not start the online survey (total excluded, $N = 89$, 17.87%). Consequently, a total of $N = 409$ participants provided data at T1. Of these 409 participants at T1, missing data were low. There were almost no missing data for any of the demographic and clinical characteristic variables, except for the number of IBD-related hospital admissions in the previous year where $N = 4$ (1%) participants provided no data. Furthermore, there were no missing data on any of the sleep outcomes at T1. For depression, anxiety, and stress at T1, $N = 19$ (5%) participants did not provide data, while $N = 25$ (6%) of participants did not provide HRQoL data. At T2, $N = 121$ (30%) were lost to follow-up, leaving a total of $N = 288$ who provided data at T2. Of these 288 participants, there were no missing data on sleep outcomes, and only $N = 2$ participants did not provide data for depression, anxiety, and stress, while $N = 3$ participants did not complete the HRQoL measure.

To test whether any baseline variables could predict subsequent loss to follow-up, we entered T1 demographic variables, sleep apnoea, insomnia, restless legs, and nightmares, as well as T1 depression, anxiety, and stress, and T1 HRQoL as independent variables into a logistic regression model, with loss to follow-up (coded as either yes or no) entered as the dependent variable. No T1 variable significantly predicted loss to follow-up at T2 at the $p < .05$ level. Furthermore, Little's MCAR test revealed that data were missing completely at random at both T1 ($X^2(368) = 326.98$, $p = .94$) and T2 ($X^2(71) = 74.76$, $p = .36$). Consequently, we are confident that the data observed at T2 are representative of the data at T1 and are unlikely subjected to attrition bias.

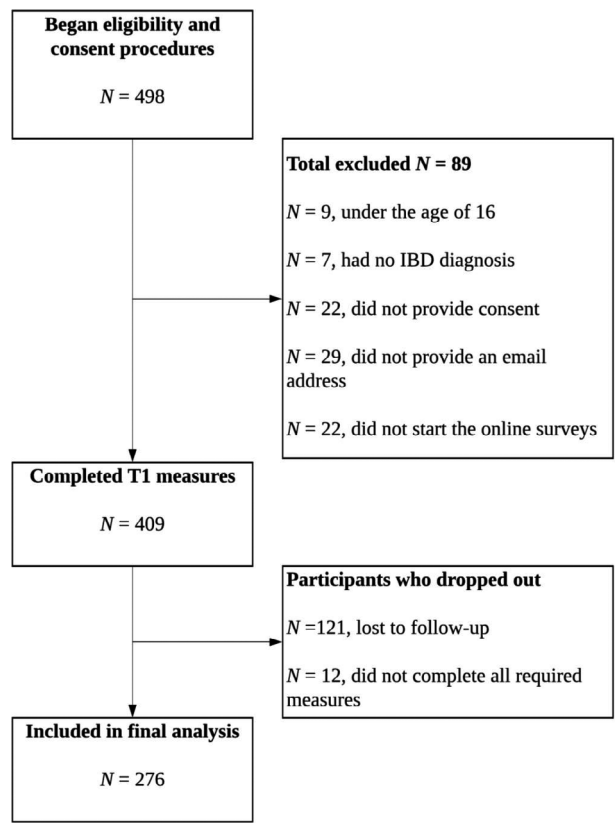


Figure 1. CONSORT diagram describing the flow of participants through the study.

Descriptive statistics

Participant demographics and clinical characteristics can be seen in Table 1. Table 2 displays descriptive statistics for symptoms of sleep apnoea, insomnia, restless legs, and nightmares along with mean symptom severity scores exceeding the clinical severity thresholds¹ for the Sleep-50 subscales proposed by Spoormaker *et al.* (2005). In order to display possible overlap between the Sleep-50 subscales, Table S1 displays the proportion of participants who exceeded the suggested clinical severity thresholds on more than one Sleep-50 domain. Table 3 displays descriptive statistics for the depression, anxiety, and stress scale. Finally, Table 4 displays descriptive statistics for total HRQoL as measured by the SIBDQ, as well as the systemic, bowel, social, and emotional subscales. We are not aware of any formal, validated normative values or cut-offs for the SIBDQ. However, to help contextualize HRQoL in the present sample, Swart, Wellsted, Lithgo, Price, and Johnson (2013) reported a mean HRQoL score of $M = 48$ (95% CI = 46.6 to 49.4) from 2,400 IBD participants in the UK. Therefore, HRQoL in the present sample was lower (worse) in comparison.

¹ It is important to note that exceeding the symptom severity threshold does not equate to a clinical diagnosis of a given sleep disorder, it simply means the participant is experiencing clinically substantive symptoms (that may or may not confer a clinical diagnosis). Diagnosis requires an assessment of the duration of symptoms, and the impact of symptoms on daily functioning that was not possible in the present research.

Table 1. Demographic and clinical characteristics at T1 and T2

Continuous variables	T1 (N = 409)		T2 (N = 276)	
	M	SD	M	SD
Age	33.86	11.57	33.48	11.36
Years living with IBD diagnosis	9.12	8.52	8.69	8.21
IBD-related hospital admissions in past year	1.62	3.92	1.51	3.82
Categorical variables	N	%	N	%
Gender				
Male	74	18	55	20
Female	335	82	221	80
IBD diagnosis				
Ulcerative Colitis (UC)	155	38	105	38
Crohn's Disease (CD)	254	62	171	62
Previous IBD-related surgery				
Yes	172	42	114	41
No	237	58	162	59
Current stoma				
Yes	58	14	42	15
No	351	86	234	85
Using immunosuppressant medication				
Yes	259	63	174	63
No	150	37	102	37
Medication for problems sleeping				
Yes	96	24	52	19
No	313	76	224	81
Therapy for problems sleeping				
Yes	21	5	14	5
No	388	95	262	95
Medication for mental health problems				
Yes	148	36	94	34
No	261	64	182	66
Therapy for mental health problems				
Yes	71	17	46	17
No	338	83	230	83

Notes. IBD = inflammatory bowel disease.

Assumption checks

Visual inspection of a scatter plot of the residuals suggested that the homoscedasticity assumption was met (i.e., residuals were randomly distributed with no clear pattern). Additionally, inspect of the Q-Q plot and histogram suggested that the dependent variable (i.e., HRQoL at T2) was normally distributed, and levels of skewness (−0.01) and kurtosis (−0.95) were low. Furthermore, collinearity of independent variables was not a concern as evidenced by Tolerance and VIF statistics falling within the acceptable ranges (tolerance ranged from 0.29 to 0.94, VIF ranged from 1.07 to 3.51). Taken together, the data used for the present analysis meet the statistical assumptions of hierarchical multiple linear regression.

Table 2. Symptom severity of sleep disturbances measured by the Sleep-50 for participants providing data at T1 and T2

Variable	Time 1 (N = 276)				Time 2 (N = 276)			
	M	SD	Cut-off exceeded ^{a,b} N (%)		M	SD	Cut-off exceeded ^{a,b} N (%)	
			Yes	No			Yes	No
Sleep apnoea	15.24	4.01	141 (51)	135 (49)	15.17	3.90	142 (51)	134 (49)
Insomnia ^c	20.34	5.87	161 (58)	115 (42)	19.88	5.46	152 (55)	124 (45)
Restless legs	7.04	2.77	132 (48)	144 (52)	7.21	2.85	141 (51)	135 (49)
Nightmares	8.38	5.62	25 (9)	251 (91)	8.72	5.65	25 (9)	251 (91)

Notes. ^aCut-off thresholds proposed by Spoormaker et al. (2005) for total scores on the Sleep-50 subscales were used to determine the proportion of participants experiencing ‘clinically substantive’ symptoms of sleep apnoea (total subscale score ≥ 15), insomnia (≥ 19), restless legs (≥ 7), and nightmares (score ≥ 3 on item 32 and total sum score ≥ 9 on items 33, 34, and 35); ^bPlease note that exceeding the threshold does not equate to a clinical diagnosis of a given sleep disorder, it simply means the participant is experiencing clinically substantive symptoms. Diagnosis requires an assessment of duration of symptoms and impact on daily function that was not possible in the present research; ^cDifferences between T1 and T2 on this variable were statistically significant ($p < .05$) based on those who provided data at both time points.

Do specific sleep disturbances at T1 predict HRQoL at T2?

Bivariate correlations between T1 sleep disturbances and T2 HRQoL can be seen in Table 5. Based on a final analysis *N* of 276 participants, we fit a hierarchical multiple linear regression model to the data (see Table 6 for an analysis summary). T1 sleep apnoea, insomnia, restless legs, and nightmares were entered as independent variables into block 1. Participant demographic and clinical characteristics that significantly correlated with T1 sleep parameters, and/or HRQoL at T2 were entered into block 2 as covariates. Finally, T1 severity of depression, anxiety, and stress, along with T1 HRQoL were entered into block 3 as covariates (for a breakdown of each model analysis step, see Table S2). The final model described in Table 6 was statistically significant ($F(13, 262) = 48.77, p < .001$), and able to explain 69% of the variance in T2 HRQoL.

T1 symptom severity of sleep apnoea ($B = -0.30, p < .05$) and insomnia ($B = -0.23, p < .05$) was significant predictors of HRQoL at T2. However, T1 restless legs ($B = -0.03, p > .87$) and severity of nightmares ($B = -0.14, p > .11$) were not significant predictors of T2 HRQoL. These results suggest that even after controlling for T1 depression, stress, and anxiety, as well as T1 HRQoL, every unit increase in sleep apnoea severity and/or insomnia at T1 was associated with a 0.30 and 0.23 unit *decrease* in HRQoL at T2 (i.e., HRQoL worsened).

Sensitivity analyses

We conducted a sensitivity analysis to explore whether possible overlap between the depression, anxiety, and stress scales and the emotional domain of the SIBDQ impacted the study findings. Correlations between the emotional subdomain of the SIBDQ and the depression ($r = -.52, p < .01$), anxiety ($r = -.43, p < .05$), and stress ($r = -.39, p < .01$) scales were statistically significant and in the small- to-medium-sized range. We

Table 3. Descriptive statistics for the depression, anxiety, and stress scales for participants providing data at T1 and T2

	Time 1 (N = 276)		Time 2 (N = 276)	
	M (SD)	N (%)	M (SD)	N (%)
Total depression ^a	7.87 (5.71)		7.43 (5.86)	
Normal range		92 (33)		112 (41)
Mild range		38 (14)		23 (8)
Moderate range		62 (22)		66 (24)
Severe range		33 (12)		28 (10)
Extremely severe range		51 (18)		47 (17)
Total anxiety	6.66 (4.85)		6.37 (4.61)	
Normal range		95 (34)		101 (37)
Mild range		22 (8)		17 (6)
Moderate range		48 (17)		63 (23)
Severe range		36 (13)		29 (11)
Extremely severe range		75 (27)		66 (24)
Total Stress ^a	9.12 (4.88)		8.66 (5.05)	
Normal range		110 (40)		124 (45)
Mild range		43 (16)		44 (16)
Moderate range		55 (20)		47 (17)
Severe range		44 (16)		39 (14)
Extremely severe range		24 (9)		22 (8)

Notes. Please see the 'The Short Form Depression, Anxiety, Stress Scale (DASS-21)' description in the measures section of the method for more detail on how cut-offs were assigned.

^aDifferences between T1 and T2 on this variable were statistically significant ($p < .05$) based on those who provided data at both time points.

Table 4. Descriptive statistics for the short inflammatory bowel disease questionnaire for participants providing data at T1 and T2

SIBDQ scores	T1 (N = 276)				T2 (N = 276)			
	M	SD	Min	Max	M	SD	Min	Max
Total HRQoL ^a	40.56	11.40	16	72	42.17	12.26	15	66
Systemic ^a	6.36	2.89	2	14	6.68	3.15	2	14
Bowel ^a	12.09	4.35	3	21	12.55	4.34	3	21
Social ^a	9.21	4.29	2	16	9.75	4.40	2	16
Emotional ^a	12.90	2.65	7	21	13.19	2.78	4	20

Notes. T1 = time 1; T2 = time 2 (4 weeks after T1); M = mean; SD = standard deviation; Min = minimum score; Max = maximum score; HRQoL = health-related quality of life; SIBDQ = Short Inflammatory Bowel Questionnaire.

^aDifferences between T1 and T2 on this variable were statistically significant ($p < .05$) based on those who provided data at both time points.

reran the regression analysis described above without the emotional subdomain included in the total IBD HRQoL score, and results remained largely the same. T1 symptom severity of sleep apnoea ($B = -0.28, p < .05$) and insomnia ($B = -0.24, p < .01$) was significant predictors of HRQoL at T2 (minus the emotional impact domain). Similarly, T1 restless

Table 5. Bivariate correlations between T1 sleep parameters and T2 health-related quality of life for participants included in the regression analysis ($N = 276$)

	1	2	3	4	5
1. T1 apnoea	1	.44**	.52**	.36**	.37**
2. T1 insomnia		1	.41**	.42**	.43**
3. T1 restless legs			1	.41**	.39**
4. T1 nightmares				1	.33**
5. T2 HRQoL					1

Notes. HRQoL = health-related quality of life.

** $p < .01$.

Table 6. Results of the hierarchical linear regression with HRQoL at T2 as the dependent variable (total analysis $N = 276$)

Variable	<i>B</i>	<i>SE</i>	95% CI (<i>B</i>)	β	<i>t</i>	<i>p</i>
Sleep disturbances at T1						
Sleep apnoea*	−0.30	0.15	−0.59 to −0.01	−0.10	−1.99	.048
Insomnia*	−0.23	0.10	−0.42 to −0.03	−0.11	−2.31	.022
Restless legs	−0.03	0.19	−0.41 to 0.34	−0.01	−0.16	.872
Nightmares	−0.14	0.09	−0.32 to 0.04	−0.07	−1.56	.121
Covariates at T1						
Depression**	−0.32	0.11	−0.54 to −0.09	−0.15	−2.78	.006
Anxiety*	−0.37	0.15	−0.67 to −0.07	−0.15	−2.45	.015
Stress***	−0.56	0.16	−0.87 to −0.25	−0.22	3.55	<.001
HRQoL***	0.69	0.05	−0.60 to 0.79	0.65	14.24	<.001
Age	0.03	0.05	−0.06 to 0.12	0.03	0.75	.456
Gender	−1.32	1.10	−3.48 to 0.85	−0.04	−1.20	.232
Year with IBD diagnosis	−0.09	0.06	−0.21 to 0.03	−0.06	−1.51	.133
Diagnosis type	−0.34	0.88	−2.07 to 1.39	−0.01	−0.39	.699
Hospital admissions	0.17	0.12	−0.07 to 0.40	0.05	1.41	.159

Note. Data reported are: *B* = unstandardized coefficient, *SE* = standard error, 95% CI (*B*) = 95% confidence intervals for standardized regression coefficient, β = standardized regression coefficient.

T1 = time 1; T2 = time 2; HRQoL = health-related quality of life; IBD = inflammatory bowel disease.

* $p < .05$; ** $p < .01$; *** $p < .001$.

legs ($B = -0.12$, $p = .474$) and severity of nightmares ($B = -0.09$, $p = .268$) were still not significant predictors. Consequently, although there was some overlap between the depression, anxiety, stress scale, and the emotional domain of the SIBDQ, this did not change interpretation of the findings.

Discussion

The present research aimed to test whether baseline symptoms of four specific types of sleep disturbances known to be associated with IBD could predict HRQoL 4 weeks later. We found that baseline symptom severity of both sleep apnoea and insomnia was

significant predictors of HRQoL 4 weeks later, even after controlling for demographic and clinical characteristics, depression, stress, and anxiety, and importantly baseline HRQoL. However, although previous research has shown that people with a diagnosis of IBD often report troubling symptoms of restless legs and nightmares (Becker *et al.*, 2018; Keefer *et al.*, 2006; Pirinen *et al.*, 2010; Ranjbaran *et al.*, 2007; Scott *et al.*, 2020; Takahara *et al.*, 2017), we found that these sleep disturbances were not predictive of subsequent HRQoL. In terms of possible explanations for this, the experience of nightmares at T1 *was* significantly associated with T2 HRQoL in each model until T1 HRQoL was added to the model as a covariate, suggesting that the experience of nightmares was unable to account for variance in HRQoL at T2 above and beyond T1 HRQoL. However, symptoms of restless legs were *never* able to predict T2 HRQoL, even in block 1 where only the other sleep parameters were included in the model (see Table S2). This might suggest that symptoms of restless legs were unable to explain variance in T2 HRQoL above and beyond the variance explained by insomnia, sleep apnoea, and nightmares. However, it is important to note that the present research measured symptoms of four types of sleep disturbance in one sample. Although bivariate associations between sleep parameters were only in the small- to-medium-sized range, there was still some overlap between sleep parameters that might have impacted results (see also Table S1). Consequently, it is possible that symptoms of restless legs and nightmares, if measured in isolation from other sleep disturbances, might predict HRQoL in those with IBD, especially in those with clinically defined restless legs and nightmares.

Sleep apnoea and insomnia as modifiable treatment targets

The findings presented here suggest that symptoms of insomnia and sleep apnoea might represent a risk factor for worse HRQoL (at least in the short term). Therefore, by reducing these sleep disturbances, we might expect that future HRQoL could be improved. The notion that improving a given sleep disturbance might lead to improvements in wider health has been applied to other areas of health (although not yet in IBD), with research generally demonstrating a benefit of improving sleep on both physical (Heckler *et al.*, 2016; Roehrs, 2009; Smith *et al.*, 2015; Vitiello, Rybarczyk, Von Korff, & Stepanski, 2009) and mental health outcomes (Christensen *et al.*, 2016; Freeman *et al.*, 2017; Scott, Webb, & Rowse, 2017). However, the application of improving sleep to IBD-related outcomes lags behind other fields. Therefore, it is unclear which types of interventions might be most effective for sleep disturbances in IBD and whether 'off the shelf' interventions for sleep disturbances might need adapting towards the needs of those with IBD. For example, cognitive behavioural therapy for insomnia (CBTi) is an effective treatment approach for insomnia (Ho *et al.*, 2015; van Straten *et al.*, 2018) and has demonstrated success in those with physical and mental health comorbidities (Wu, Appleman, Salazar, & Ong, 2015). However, given that people with IBD often experience physical symptoms that interfere with getting a good night's sleep (e.g., abdominal pain, needing to use the toilet), as well as an increased prevalence of mental health difficulties (Brooks *et al.*, 2019; Tribbick *et al.*, 2015) that are often associated with more problems sleeping, it is important that CBTi for those with IBD accounts for this. We recommend that future research should focus on conducting high-quality randomized controlled trials testing the effect of interventions designed to improve sleep, particularly insomnia and sleep apnoea, on subsequent IBD HRQoL. Doing so will not only provide an evidence base from which clinicians and policy makers can identify effective interventions to improve sleep disturbances in IBD (an area that is

currently lacking), but will also provide a robust causal test of the role of sleep disturbances in the trajectory of HRQoL (Cartwright, 2010).

The present research is the first (to our knowledge) to report the prospective association between specific sleep disturbances and HRQoL in those with IBD. However, it is important to note that evidence that poor sleep can predict HRQoL does not preclude the reverse direction and that more impaired HRQoL is likely to *also* lead to more problems sleeping (i.e., a bidirectional relationship). Indeed, given that the relationship between sleep and health and well-being has been shown to be bidirectional in non-IBD populations (Alsaadi *et al.*, 2014; Alvaro *et al.*, 2013; Bartlett & Jackson, 2016; Lee, Buxton, Andel, & Almeida, 2019; Van Dyk, Thompson, & Nelson, 2016), it is likely that the relationship between sleep and IBD HRQoL is also bidirectional. The present research was unable to inform the bidirectional nature of this relationship; therefore, future research might consider developing the present study by examining the bidirectional relationship between specific sleep disturbances and HRQoL so that the relationship can be better understood. Furthermore, because the present study did not measure IBD symptom activity directly, it is difficult to rule out that the symptoms of IBD itself might be a common cause of both lower HRQoL and problems sleeping simultaneously. Although disease symptom activity has been shown to contribute only 37% of the variance in IBD HRQoL (van der Have *et al.*, 2014), and the bowel symptom subscale of the SIBDQ (which correlates strongly with disease activity, Jowett *et al.*, 2001) was entered as a covariate in the regression model as part of the HRQoL total score, future research should consider employing a more direct measure of IBD symptom activity so that the independent effect of insomnia and sleep apnoea might be better isolated.

The importance of screening for specific sleep disturbances in routine care

The present findings suggest that the routine care of those with IBD could consider incorporating assessments to screen for the presence of specific types of sleep disturbances (particularly insomnia and sleep apnoea). However, the routine management of sleep disturbances in IBD is not common place, and part of the problem might be the lack of clear guidance on screening and treating sleep disturbances. For example, there are many types of screening tools that can be either self-reported by participants or objectively measured using technology that can be used to detect sleep disturbances ranging from global measures of sleep quality, to tools to detect specific sleep disturbances like insomnia and sleep apnoea. Currently, there are few guidelines for the management of sleep disturbances in IBD (National Institute for Health & Care Excellence, 2019a, 2019b), meaning patients and professionals might lack the information they need to make informed decisions around how to detect sleep disturbances (and therefore how to treat sleep disturbances). Consequently, we recommend that future research should consider investigating the possible barriers to the routine management of sleep disturbances in IBD from both the perspectives of health care professionals and patients. Doing so will allow the identification of factors that preclude the effective management of sleep so that they can be ameliorated.

Limitations

Firstly, recruitment to the present research was based on self-reported IBD diagnosis from a national IBD charity and online IBD support groups. Although Randell *et al.* (2014)

reported that agreement between self-reported diagnosis and clinician confirmation of diagnosis is high at 97% (see also Kelstrup, Juillerat, & Korzenik, 2014), future research might seek to include clinically confirmed IBD cases. Secondly, although there is evidence that IBD is more prevalent in females (Brant & Nguyen, 2008), and the present research controlled for gender in the analysis, the majority of the sample were female; therefore, the representativeness of the present findings to male IBD populations could be considered limited. Finally, the present research employed a single, relatively short follow-up period of 4 weeks. It would be interesting for future research to conduct similar studies using multiple, longer follow-up durations so that the impact of problems sleeping on long-term HRQoL in IBD can be better understood, as well as examining a bidirectional association between sleep and HRQoL. Indeed, little is known about the trajectory of sleep disturbances experienced by those with IBD in general, and being able to better characterize the nature and course of sleep disturbances in IBD would be a useful addition to the literature.

Conclusion

In conclusion, the present research suggests that higher symptom severity of sleep apnoea and insomnia (but not restless legs or nightmares) is longitudinally associated with poorer HRQoL in those with IBD. These findings suggest that experiences of sleep apnoea and insomnia could represent modifiable behavioural treatment targets in addition to routine IBD care that could confer particular benefits to the HRQoL. However, future research might consider examining the temporal relationship between sleep disturbances and HRQoL over longer time periods than those reported here so that the trajectory of sleep disturbances, and their impact on IBD outcomes can be better understood over the longer term. We believe the next appropriate steps in the field are to test whether interventions designed to improve sleep, particularly symptoms of sleep apnoea and insomnia, are not only able to improve sleep in those with IBD, but also whether any improvement in sleep leads to improvements in IBD-related outcomes such as HRQoL.

Conflicts of interest

All authors declare no conflict of interest.

Author contributions

Alexander J. Scott (Conceptualization; Data curation; Formal analysis; Methodology; Project administration; Supervision; Writing – original draft; Writing – review & editing) Olivia Flowers (Conceptualization; Investigation; Methodology; Project administration; Writing – review & editing) Georgina Rowse (Conceptualization; Supervision; Writing – review & editing)

Data availability statement

Data for this article is publicly available online at the following doi: 10.15131/shef.data.12504815

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Supporting Information

The following supporting information may be found in the online edition of the article:

Table S1. Proportion of participants providing data at T1 and T2 that also exceed symptom cut-offs for more than one concurrent sleep disturbance (total $N = 276$)

Table S2. Full results from each analysis step of the hierarchical linear regression with HRQoL at T2 as the dependent variable (total analysis $N = 276$)